UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,792	07/28/2003	Jon A. Wolff	Mirus.040.01	5528

25032 7590 08/06/2007

MIRUS CORPORATION
505 SOUTH ROSA RD
MADISON, WI 53719

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/628,792	WOLFF ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *15,20,22,24 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-14,16-19, 21,23,25,26,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on July 02, 2007 is acknowledged. Claims 1-30 are pending in this application.

Restriction

1. Applicant's election of Group 1 (claims 9-10), drawn to a process for delivering a molecule to an extravascular cell in a mammalian tissue wherein the molecule consists of a protein/peptide and the election of hypertonic solution in the reply filed on July 02, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claim 11 is withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention, there being no allowable generic or linking claim. Claim 28 is withdrawn from further consideration, as being drawn to nonelected species. Claims 15, 20, 22, 24 and 27 are withdrawn from further consideration as being drawn to species not directed to prior art species. Claims 1-10, 12-14, 16-19, 21, 23, 25-26 and 29-30 read on species of prior art. Claims 1-10, 12-14, 16-19, 21, 23, 25-26 and 29-30 are examined on the merits in this office action.

Minor Informalities

2. The title is objected to because the title is too long. The title is limited to 2-7 words maximum. A new title is required that is clearly indicative of the invention to which the claims are directed.

Rejection-35 U.S.C. 112, 2nd

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10, 12-14, 16-19, 21, 23, 25-26 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. The base claim 1 recites "...the volume of the injection solution and the rate of injection solution insertion..." The phrase "rate of injection solution insertion" is unclear. A rate implies that there is a standard of time that is compared to. For example, a rate can be 0.001 ml per second and so on. Furthermore, a rate of injection can be continuous as in intravenous injection. Thus, "rate of injection solution insertion" is unclear as recited in the claim.

Rejection-35 U.S.C. 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-7, 9-10, 12-13, 21, 23 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al (US Patent # 5346696).

8. The instant claims are drawn to a process for delivering a molecule to an extravascular cell in a mammalian tissue in vivo, wherein the volume of the injection solution and the rate of injection solution insertion result in transient increased tissue size and extravascular fluid volume within the tissue, extravasation of the molecule and delivery of the molecule to the extravascular cell, wherein fluid flow out of the target tissue is occluded and insertion of the injection solution results in increased permeability of vessels in the tissue to the molecule. Furthermore, the claims are drawn to the molecule consists of a biologically active compound consisting of a macromolecule (protein/peptide) that is greater than 5 kDa and greater than 30 kDa.

9. Kim et al teach conjugated medicinal agent prepared by combining asialoglycoprotein with a medicine which acts specifically on the liver (see abstract). Further, the reference teaches that the conjugated medicinal agent also includes a conjugated interferon antiviral agent prepared by combining asialoglycoprotein with recombinant interferon (INF) (see column 1, lines 6-11). As evidenced by Tanabe et al (J. Biol. Chem., 1979, 254(4): 1038-1043) the molecular weight of asialoglycoprotein is 47,000 Da (see p. 1041, left column, 1st paragraph). Thus, this reads on claims 4-7, 9-10 and 12-13. The reference further teaches that in order to determine the survival of intravenously injected desialyated plasma proteins, alpha(1)-acid glycoprotein

(asialoororosomucoid) was injected in the tail vein of male albino rats...samples of blood were taken at varying time intervals from the tail veins in heparinized tubes and centrifuged...animals were sacrificed, their liver was removed at the times and aliquots were used for determination of radioactivity (see column 10, lines 20-44). This reads on claims 1-3, 21, 23 and 30. It is inherent that once an injection of solution containing molecule is made into the lumen (vein), there is transient increase in tissue size at the site of injection and as the solution is being carried into the target tissue by the blood stream, due to the injection of the solution, and the extravascular fluid volume within the tissue would also increase. Furthermore, injection of solution would inherently increase the permeability of the vessels in the tissue to the molecule.

10. Claims 1, 14, 16, 17, 25, 26, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Veech RL (US Patent # 4663166).

11. The instant claims are drawn to a process for delivering a molecule to an extravascular cell (liver cell) in a mammalian tissue in vivo comprising: inserting an injection solution containing the molecule into the lumen of a vessel wherein the volume of the injection solution and the rate of injection solution insertion result in transient increased tissue size and intravascular fluid volume within the tissue, extravasation of the molecule and delivery of the molecule to the extravascular cell and wherein the injection solution contains a compound that increase vessel permeability and the injection solution is hypertonic. Furthermore, the claims are drawn to the injection solution containing less than 20 mM salt.

12. Veech RL teaches electrolyte solutions which are useful in electrolyte and fluid therapy, parenteral nutrition, and dialysis (see abstract). This reads on claims 1 and 30. The reference teaches that the solution contains about 1.24 to 1.6 mM (preferred 1,36 to 1.5 mM NaCl) NaCl for hemo and peritoneal dialysis solutions (see Tables VI and VII). Table XVII teaches a composition of fluids (see column 68). Furthermore, the reference teaches that Class II solutions are useful in dialysis, peritoneal, ambulatory peritoneal dialysis or hemodialysis (see column 34, lines 1-2) and a physician may henceforth wish to administer normal or hypertonic saline solution (see column 34, lines 7-13). Furthermore, the reference teaches that solutions of Class II can be used as such, or can be employed as diluent for plasma extenders or for reconstituted frozen blood. For example, dehydrated plasma can be dissolved and dispersed in a solution of class II so as to produce an injectable solution (see column 34, lines 14-18). This reads on claims 14, 16, 17, 23-26 and 29. Furthermore, the reference teaches liver nutrition and perfusion to the liver (see Table I and Example 43). It is inherent that once an injection of solution containing molecule is made into the lumen (vein), for example for dialysis or i.v., there is transient increase in tissue size at the site of injection and as the solution is being carried into the target tissue by the blood stream, due to the injection of the solution, and the extravascular fluid volume within the tissue would also increase. Furthermore, injection of solution would inherently increase the permeability of the vessels in the tissue to the molecule.

13. Claims 1 and 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Donovan S (US Patent # 6143306).

14. The instant claims are drawn to a process for delivering a molecule to an extravascular cell in a mammalian tissue in vivo comprising: inserting an injection solution containing the molecule into the lumen of a vessel wherein the volume of the injection solution and the rate of injection solution insertion result in transient increased tissue size and intravascular fluid volume within the tissue, extravasation of the molecule and delivery of the molecule to the extravascular cell and the molecule is a macromolecule having molecular weight greater than 500 kDa.

15. Donovan S teaches that the molecular weight of botulinum toxin protein molecule is about 150 kD; however, the botulinum toxins are released by Clostridial bacterium as complexes comprising the 150 kD botulinum toxin protein molecule along with associated non-toxic protein. The botulinum toxin complexes can be produced by *C. bacterium* as 900 kD, 500 kD and 300 kD forms. The non-toxin proteins may act to provide stability against denaturation to the botulinum toxin molecule and protection against digestive acids when toxin is ingested. The larger (greater than about 150 kD molecular weight) botulinum toxin complexes may results in a slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection of a botulinum toxin complex (see column 5, lines 31-55). This reads on claims 1 and 5-8. It is inherent that once an injection of solution containing molecule is made into the lumen, there is transient increase in tissue size at the site of injection and as the solution is being carried into the target tissue by the blood stream, due to the injection of the solution,

and the extravascular fluid volume within the tissue would also increase. Furthermore, injection of solution would inherently increase the permeability of the vessels in the tissue to the molecule.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1, 18, 19 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Voet et al (US Patent # 6821520).

17. The instant claims are drawn to a process for delivering a molecule to an extravascular cell in a mammalian tissue (skeletal muscle cell) in vivo comprising: inserting an injection solution containing the molecule into the lumen of a vessel wherein the volume of the injection solution and the rate of injection solution insertion result in transient increased tissue size and intravascular fluid volume within the tissue, extravasation of the molecule and delivery of the molecule to the extravascular cell.

18. Voet et al teach methods for treating by local administration of a Clostridial toxin, such as a botulinum toxin, to the gland of a patient (see abstract). The claim further teaches that both liquid stable formulations and pure botulinum toxin formulations are known (see column , lines) and typically, a Clostridial toxin is administered locally and directly into a target tissue, such as a skeletal muscle, by intramuscular or subcutaneous injection (see column , lines). This reads on claims 1, 18-19 and 30. It is inherent that once an injection of solution containing molecule is made into the lumen,

there is transient increase in tissue size at the site of injection and as the solution is being carried into the target tissue at the site of injection (in this instant, directly into a target tissue). Furthermore, the extravascular fluid volume within the tissue would also increase, and injection of solution would inherently increase the permeability of the vessels in the tissue to the molecule.

Conclusion

16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Julie Ha
Patent Examiner
AU 1654

8/1/08
ANISH GUPTA
PRIMARY EXAMINER